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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/722,010	11/27/2000	Kuen Yong Lee	UMICH-9	4013

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EXAMINER

MAIER, LEIGH C

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 11/25/2002

5

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/722,010

Applicant(s)
Lee

Examiner
Leigh Maier

Art Unit
1623



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Sep 6, 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above, claim(s) 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 and 18 is/are rejected.
- 7) ☒ Claim(s) 17 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

Election/Restriction

Applicant's election without traverse of Group I, with the specific election of a synthetic alginate, in Paper No. 4 is acknowledged. Claims 1-18 read on the elected species. Claim 19 is withdrawn from consideration as being drawn to a non-elected species.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "[a] hydrogel composition comprising a hydrogel polymer reacted with an excess amount of cross-linker. . ." The specification defines "hydrogel" as a "three-dimensional network of cross-linked hydrophilic polymers comprising water." See page 5, lines 24-26. Therefore, it is not clear if the claim intends (1) a hydrogel polymer prepared by treating a hydrophilic polymer with an excess amount of cross-linker or (2) a hydrogel polymer - a polymer that is already cross-linked, by definition - that is further treated with more cross-linker. The claims are rendered vague and indefinite.

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The claim further recited that the polymer “has a *significant extent* of cross-links to other hydrogel molecules and also has a *significant extent* of cross-links with at least one functional group bound. . .and at least one unbound functional group. . .” (Emphasis added) The term “significant extent” does not appear to have a particular definition in the specification. As described in the specification, the invention appears to be drawn to a cross-linked hydrogel having some measurable number of “dangling” cross-linker molecules. It is not clear if this is what is being claimed or if some particular amount or ratio is required. The claims are thus rendered vague and indefinite.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by MOONEY et al (WO 98/12228).

MOONEY discloses the preparation of a hydrogel comprising the treatment of polyaldehyde guluronate (PAG) with adipic dihydrazide (AAD), resulting in a cross-linked

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hydrogel. See example 19. The reference is silent regarding the existence of unbound cross-linkers. However, a comparison of the preparation of the product in the reference and the instant product supports the existence of unbound cross-linkers in the MOONEY product. The instant disclosure describes the preparation of PAG having a degree of oxidation of 655 as the starting material. See page 8, lines 25-34. A 20 wt% solution of this product is treated with AAD concentrations of from 50 mM to 250 mM. See page 9, lines 27-30. In example 19, MOONEY describes treating 6 wt% solution of PAG with 150 mM of AAD. At constant degree of oxidation, the MOONEY process would certainly result in excess crosslinker relative to the starting aldehydes: A 6 wt% solution of PAG would have fewer aldehydes than a 20 wt% solution. Although MOONEY is silent regarding the precise degree of oxidation of the PAG, the reference notes that crosslinked 20% oxidized PAG exhibited weak gels, and 80% oxidized PAG provided stiff and brittle material. See page 58, lines 1-3. Therefore it appears that the exemplified PAG in MOONEY is comparable in degree of oxidation to the instant PAG, so that the MOONEY process would be expected to have excess crosslinker, providing some number of partially bound or "dangling" crosslinkers. This process would be expected to have the same crosslinking efficiency as recited in the instant claims.

The reference is silent regarding the molecular weight of the PAG. However, the reference describes the preparation of the precursor PG from alginate (See page 55, lines 1-6) in the same manner as in the instant specification. See page 8, lines 10-16. It would be expected that

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the resulting PG would have the same or similar molecular weight, of around 7000 kD, which is below the renal threshold of about 30-50 kD. See MOONEY at page 17, lines 5-8.

The reference is silent regarding the initial shear modulus recited in the instant claims. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.d. 1252, 195 USPQ 430 (CCA 1977) and *In re Fitzgerald*, 619 F.d. 67, 205 USPQ 594 (CCA 1980). However, MOONEY does report compressive modulus values for the hydrogel products. One product, for example at page 56, lines 5-10, is reported to have a compressive modulus of 560 kPa. Given that the shear modulus is generally a small fraction of the compressive modulus, it would be expected that the shear modulus of the disclosed product would fall into the range recited in claims 13 and 14.

MOONEY further discloses the methods recited in claim 15. See example 22. The method requires only “administering” the hydrogel composition.

Claims 1-16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by BOUHADIR et al (Polymer, 1999).

BOUHADIR discloses the preparation of a hydrogel comprising the treatment of PAG (derived from PG having MW of 6000 D) with adipic dihydrazide (AAD), resulting in a cross-linked hydrogel with partially reacted crosslinkers. See sections 3.1 and 3.2 and Fig. 4.

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The reference discloses crosslinking efficiencies of 84 to 96%. However, from the data in the figure, it appears that BOUHADIR is using a different definition of crosslinking efficiency. The reference appears to measure crosslinking efficiency as the amount of fully bonded crosslinker, whereas the instant specification appears to refer to the amount of single-end dangling crosslinkers based on the total amount of reacted crosslinker. See specification at page 4, lines 18-21. At 300 mM in Fig. 4, there appears to be >20% dangling crosslinkers compared with the total amount of bound crosslinker.

The reference is silent regarding the initial shear modulus recited in the instant claims. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.d. 1252, 195 USPQ 430 (CCA 1977) and *In re Fitzgerald*, 619 F.d. 67, 205 USPQ 594 (CCA 1980). However, BOUHADIR discloses compressive modulus values for products ranging from 82 kPa to 1000 kPa. Given that the shear modulus is generally a small fraction of the compressive modulus, it would be expected that the shear modulus of the disclosed products would fall into the range recited in claims 13 and 14.

As noted above the method recited in claim 15 requires only “administering” the hydrogel composition which would include “administering” the hydrogel to the laboratory apparatus used to measure physical properties, such as compressive modulus.

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Conclusion

The art of record does not teach a hydrogel composition comprising a synthetic alginate modified to contain hydrazide groups and crosslinked with a crosslinker comprising at least two aldehyde groups.

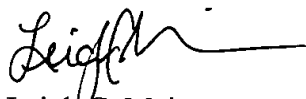
Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Tuesday, Wednesday, or Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Visit the U.S. PTO's site on the World Wide Web at <http://www.uspto.gov>. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.



Leigh C. Maier
Patent Examiner
November 15, 2002